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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/535,433	02/02/2006	Lorenzo Frigerio	1009-0118PUS1	8447

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EXAMINER

BRISTOL, LYNN ANNE

ART UNIT	PAPER NUMBER
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1643

SHORTENED STATUTORY PERIOD OF RESPONSE	NOTIFICATION DATE	DELIVERY MODE
31 DAYS	02/02/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Notice of this Office communication was sent electronically on the above-indicated "Notification Date" and has a shortened statutory period for reply of 31 DAYS from 02/02/2007.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No. 10/535,433	Applicant(s) FRIGERIO ET AL.	
	Examiner Lynn Bristol	Art Unit 1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is FINAL. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1 and 34-81 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☐ Claim(s) ____ is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☒ Claim(s) 1 and 34-81 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date ____ | 6) <input type="checkbox"/> Other: ____ |

DETAILED ACTION

1. Claims 1 and 34-81 are all the pending claims for this application and all the claims subject to lack of unity restriction.
2. Claims 36, 45, 55, 62 and 63 are drawn to the formula “-(Xaa₁)_m C(Xaa₂)_n”. Applicants are requested to elect a single number for each of “m” and “n” in addition to the amino acid residues for each of Xaa₁ and Xaa₂.
3. Claims 40, 56 and 57 are drawn to amino acid sequences \geq four (4) amino acids in length, and require sequence identifiers pursuant to 37 CFR 1.821 (c) and/or (d):

Claim 40: X₁ X₂ X₃ V S X₄

Claim 56: X₁ X₂ X₃ V S X₄

Claim 57: X₁ X₂ X₃ V S X₄.

Applicants are required to identify the above-referenced sequences with sequence identifiers in addition to any other sequences that may not be properly identified.

4. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

To have a general inventive concept under PCT rule 13.1, the inventions need to be linked by a special technical feature. The special technical feature recited in claim 1 is an antibody molecule containing a heavy chain comprising a modification in the $\alpha 3$ or μ domain, where the modification occurs within the C-terminus 18 amino acids in order to remove or reduce the effectiveness of vacuolar targeting signal sequences. In

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view of this, the combination of Frigerio et al. (Plant Physiology 123:1483-1493 (August 2000); cited in the IDS of May 18, 2005), Vitale and Raikhel (Trends in Plant Science 4(4):149-155 (April 1999); cited in the IDS of May 18, 2005)) and Koide et al. (Plant Cell Physiol. 40(11):1152-1159 (1999)) reads on the technical feature of the invention.

Frigerio discloses that vacuolar delivery of sIgA (C-alpha 2 and C alpha 3)/G in plants is mediated by the alpha domains present in the hybrid alpha/gamma-heavy chains and indicates that plant secretory system recognizes cryptic vacuolar signaling domain in that delivers the hybrid molecule to the vacuole rather than being secreted. Frigerio discusses several vacuolar signaling domains recognized in other plant proteins and which may bear homology to the alpha domain.

Vitale and Raikhel disclose peptides involved in the sorting of soluble vacuolar proteins which comprise VS or SV repeats and are found, for example, in C-terminal propeptides of plants.

Koide discloses the VS and SV repeats in potato PT20 protein as important in vacuolar trafficking of the protein.

The references result in rendering the invention obvious because it would have been obvious to combine the teachings to produce the claimed technical feature by substituting or deleting residues in the C-terminal portion of the alpha domain in order to reduce the effectiveness of vacuolar targeting because in modifying the C-terminal portion of the hybrid protein, the amount of secreted protein would have been increased. Therefore the technical feature recited in claim 1 is not special. Accordingly the groups are not so linked as to form a single general concept under PCT Rule 13.1.

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5. In accordance with 37 CFR 1.499, applicant is required, in response to this action, to elect a single invention to which the claims must be restricted.

Group 1, claim(s) 1, 34-44, 46, 48, 50 and 52, drawn to a method of making an antibody with a modified heavy chain alpha 3 or mu domain comprising modifying the the C-terminus 18 amino acid residues in order to reduce or eliminate the vacuolar targeting of the antibody.

Group 2, claim(s) 45, 47, 49, 51 and 53, drawn to a method of adding a J-chain binding capability to the heavy chain of an antibody by introducing a synthetic tail comprising amino acid sequence $-(Xaa_1)_m C(Xaa_2)_n$.

Group 3, claim(s) 54, 56, 58, 60, 62, 64 and 66, drawn to an antibody having a C-terminus modified heavy chain comprising an alpha 3 or mu domain lacking one or more targeting signals.

Group 4, claim(s) 55, 57, 59, 61, 63, 65 and 67, drawn to an antibody comprising $-(Xaa_1)_m C(Xaa_2)_n$ and capable of binding to a J-chain.

Group 5, claim(s) 68, drawn to a method of treating a disease comprising administering an antibody having a C-terminus modified heavy chain comprising an alpha 3 or mu domain lacking one or more targeting signals.

Group 6, claim(s) 69, drawn to a method of treating a disease comprising administering an antibody comprising $-(Xaa_1)_m C(Xaa_2)_n$ and capable of binding to a J-chain.

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Group 7, claim(s) 70, drawn to a method of prophylaxis comprising administering an antibody having a C-terminus modified heavy chain comprising an alpha 3 or mu domain lacking one or more targeting signals.

Group 8, claim(s) 71, drawn to a method of prophylaxis comprising administering an antibody comprising $-(Xaa_1)_m C(Xaa_2)_n$ and capable of binding to a J-chain.

Group 9, claim(s) 72, 74 and 76, drawn to vectors and host cells comprising nucleotides encoding an antibody having a C-terminus modified heavy chain comprising an alpha 3 or mu domain lacking one or more targeting signals.

Group 10, claim(s) 73, 75 and 77, drawn to vectors and host cells comprising nucleotides encoding an antibody comprising $-(Xaa_1)_m C(Xaa_2)_n$ and capable of binding to a J-chain.

Group 11, claim(s) 78, drawn to a transgenic plant comprising a nucleotide encoding an antibody having a C-terminus modified heavy chain comprising an alpha 3 or mu domain lacking one or more targeting signals.

Group 12, claim(s) 79, drawn to a transgenic plant comprising a nucleotide encoding an antibody comprising $-(Xaa_1)_m C(Xaa_2)_n$ and capable of binding to a J-chain.

Group 13, claim(s) 80, drawn to an immunoassay comprising an antibody having a C-terminus modified heavy chain comprising an alpha 3 or mu domain lacking one or more targeting signals.

Group 14, claim(s) 81, drawn to an immunoassay comprising an antibody comprising $-(Xaa_1)_m C(Xaa_2)_n$ and capable of binding to a J-chain.

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6. The inventions listed as Groups 1-14 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: As set forth above, in view of the teaching of Frigerio et al., Vitale and Raikhel and Koide et al., the groups are not so linked as to form a single general concept under PCT Rule 13.1 because the technical feature of claim 1 is not special.

7. The methods of Groups 1, 2, 5-8, 13 and 14 differ in the method objectives, method steps, intended populations and parameters and in the reagents used. The method of Group 1 requires an antibody having an alpha 3 or mu chain domain and a nucleotide encoding the chain, and introducing any modification anywhere in the C-terminal 18 amino acids of the domain in order to reduce or eliminate vacuolar targeting signal sequences and further expressing the antibody from a host cell; the method of Group 2 requires a nucleotide sequence for a heavy chain and introducing a tail sequence comprising amino acids $-(Xaa_1)_m C(Xaa_2)_n$, in order to add a J-chain binding capability to the heavy chain of the antibody; the method of Group 5 requires a patient having any disease and an antibody having a C-terminus modified heavy chain comprising an alpha 3 or mu domain lacking one or more targeting signals, and administering the antibody in order to treat the disease; the method of Group 6 requires a patient having any disease and an antibody comprising $-(Xaa_1)_m C(Xaa_2)_n$ and capable of binding to a J-chain, and administering the antibody in order to treat the disease; the method of Group 7 requires a patient or animal and an antibody having a C-terminus modified heavy chain comprising an alpha 3 or mu domain lacking one or

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more targeting signals, and administering the antibody in order to achieve prophylaxis; the method of Group 8 requires a patient or animal and an antibody comprising $-(Xaa_1)_m$ C(Xaa₂)_n and capable of binding to a J-chain, and administering the antibody in order to achieve prophylaxis; the method of Group 13 requires any immunoassay and an antibody having a C-terminus modified heavy chain comprising an alpha 3 or mu domain lacking one or more targeting signals; and the method of Group 14 requires any immunoassay and an antibody comprising $-(Xaa_1)_m$ C(Xaa₂)_n and capable of binding to a J-chain. The examination of all groups would require different searches in the U.S., foreign and international patent literature and the scientific literature and would require the consideration of different patentability issues. Thus the methods of Groups 1, 2, 5-8, 13 and 14 are separate and distinct in having different method steps, different intended populations and different endpoints and are patentably distinct.

8. Inventions of Groups 3, 4 and 9-12 represent separate and distinct products which are made by materially different methods, and are used in materially different methods which have different modes of operation, different functions and different effects. Groups 3 and 4 are antibodies, Groups 9 and 10 are nucleic acids, and Groups 11 and 12 are transgenic plants. As between the antibodies, each is structurally and functionally independent and distinct for the following reasons: each antibody has a unique amino acid sequence, each antibody has a different modified heavy chain domain which confers a different property on the molecule, and each antibody binds to a different epitope and each antibody has its own unique ability to stimulate an immune response and/or binding affinity to an antigen or epitope. The antibody proteins, the

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nucleic acids and the transgenic plants are all structurally and functionally distinct. The examination of all groups would require different searches in the U.S., foreign and international patent literature and the scientific literature and would require the consideration of different patentability issues. Thus the products of Groups 3, 4 and 9-12 are separate and distinct in having different structural and functional properties and are patentably distinct.

9. Inventions of Group 3 and Groups 5, 7 and 13; Group 4 and Groups 6, 8 and 14; Group 9 and Group 11; and Group 10 and group 12 are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the method of treating a disease or producing prophylaxis can be practiced with a materially different product such as chemotherapy, small molecule drugs, nucleic acids strategies such as anti-sense or DNA vaccines, etc. As for the immunoassay, it can be practiced with a materially different reagent such as a ligand or a protein or another antibody. As for the transgenic plant, a transgenic plant can be produced with another materially different nucleic acid or recombinant construct.

10. Inventions of Groups 1 and 3; and Groups 2 and 4 are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make another and materially different product or (2) that the product as claimed can be made by another

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and materially different process (MPEP § 806.05(f)). In the instant case the process of Group 1 can be used to make materially different proteins such as any modified non-antibody protein containing a vacuole signaling sequence that otherwise accumulates in the vacuole. As for the process of Group II any protein could have a J-chain inserted to produce a dimeric protein with improved secretory properties.

10. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

11. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lynn Bristol whose telephone number is 571-272-6883. The examiner can normally be reached on 8:00-4:00, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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